AdA 211921

20030203117

EFFECTS OF EXERCISE INTENSITY AND PRE-EXERCISE FEEDING
ON SPLANCHNIC TISSUE BLOOD FLOW

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SUMMARY

Difficulties in comparing studies, potentially causing many apparent discrepancies, have arisen from variations in EX intensity, EX duration, thermal responses to EX. and uncertainties regarding training and feeding status. We have demonstrated generalized declines in blood flows (BFs) to the gastrointestinal organs, spleen and kidney, with no change in liver BF in fasted untrained swine during graded exercise. These changes in visceral organ BFs were associated with progressive increments in heart rate, cardiac output, mean arterial pressure, left ventricular BF, and active muscle BF. Postprandial EX produced similar reductions in stomach and intestine BFs compared to resting values, but BFs were maintained consistently higher than for corresponding fasting EX. Postprandial near maximal EX resulted in an increased hepatic artery blood flow, indicating activity of some vasodilatory mechanism not functioning in the fasted condition, and possibly demonstrating the 'hepatic arterial buffer response' (20). Postprandial EX also resulted in higher cardiac outputs, but lower active muscle BFs than for fasting EX. This information suggests a neurogenic autonomic reflex of gastrointestinal origin may be active in minimizing BF to organs when the additional stress of digestion is superimposed on the stress of exercise. This reflex appears to redirect blood away from active tissues in order to preserve the higher splanchnic blood flows required for digestion and absorption. These data confirm the importance of controlling for exercise intensity and pre-exercise feeding status when measurements of tissue BF or central cardiovascular variables are of interest.

INTRODUCTION

The effects of feeding and exercise (EX) have been shown to produce competing effects on splanchnic or gastrointestinal (GI) blood flow (BF). However, several reports have presented conflicting data. Several studies have reported that feeding increases splanchnic BF (SBF) at rest (7,11,16,26, 27,29), with the increased BF correlated with the increased demands of the digestive and absorptive processes (7). Exercise has produced a diminution of gastric secretions (19) and decreased SBF (2,3,4,21,24,25,28,30,31), while others have found no change in SBF (11,16,32,34). Postprandial EX has similarly reduced SBF compared to resting values (3,11,35), while some authors have reported no change (16,36). Additionally, postprandial EX has been found to produce higher heart rates and blood pressures compared to fasting EX (12), while others have reported no differences (11,18). Prior consumption of a mixed meal (8) or hypertonic solution (10) has produced little effect on gastric secretion or emptying during EX. These data indicate that GI-BF requirements for digestion may be preserved, even with coincident exercise stress.

Several factors may have contributed to the observed variations in BF responses to postprandial EX. Meal composition (fat, carbohydrate, protein) has been shown to profoundly effect the BF response to a meal (27,33,37). Transient alterations in splanchnic BF have been demonstrated at the onset of EX with continued variations over time (2,3,9,11,16). Therefore, the timing of BF measurements may have effected the reported response. The effects of EX duration on the cardiovascular and BF responses to exercise will be addressed more completely in a subsequent paper (13).

Discrepancies among these studies may have been related to variations in unreported differences in experimental conditions (24), which were previously considered to have insignificant potential affects on results. Difficulties in the interpretation of splanchnic BF data have been further confounded by either incomplete (31,35) or omitted subject feeding information (1,2,4,9,24, 28,32,34). Therefore, variation in feeding status (e.g., type of food, meal timing, or amount consumed) may have substantially affected splanchnic BF responses to EX. Additionally, as fasted EX intensity (1,23,24,31,35) or thermal stress (2,30,31) increased, the EX induced reduction in splanchnic BF was greater. Quantification of EX intensity was difficult to assess in some studies (3,11,13,26,31,35), while thermal responses were not reported by

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others (3,4,5,9,11,16,21,23,24,25,34,35). Differences in cardiovascular reserve or exercise capacity may also have contributed to variations in splanchnic BF responses to EX, as endurance trained subjects had different splanchnic BF responses than untrained controls (5,23,25).

Many unanswered questions exist regarding interactions among the various antagonistic control mechanisms which regulate GI blood flow (8,29,30,38,41). The balance of these control mechanisms determines both cardiovascular and metabolic homeostasis during EX. More information on the contribution of these factors to overall cardiovascular regulation is needed to enable us to differentiate the causes of observed variations. The purpose of this study was to examine the interaction of EX intensity and pre-exercise feeding on visceral organ blood flows and cardiovascular variables.

METHODS

Progressive intensity exercise (EX) tests were performed by untrained miniature swine familiarized with running on a treadmill to evaluate their cardiovascular and tissue blood flow (BF) responses. Exercise intensities were selected to produce nearly matched heart rates among animals at two submaximal workloads in order to compare myocardial work at the matched heart rates. Some of the pigs were fed prior to the EX tests to evaluate the effects of pre-exercise feeding on gastrointestinal (GI) BF.

Subjects. Thirty, 9-12 month old Yucatan miniature swine weighing 40.1 ± 0.7 Kg were studied. There were no differences between groups in age or weight. Each animal was familiarized with running on a motor-driven tread-mill at moderate intensities, 10 to 15 minutes per day, for a two week period prior to surgery.

Surgical Instrumentation. Anesthesia was induced by intramuscular ketamine (25 mg·Kg^{-1}) and atropine (2 mg), followed by intravenous sodium thiamylal (25 mg·Kg^{-1}). After intubation with an endotracheal tube, surgical anesthesia was maintained by halothane (1-2%). A left thoracotomy via the fourth or fifth intercostal space was performed to implant silastic catheters in the left atrium, descending aorta, and pulmonary artery. The silastic catheters were constructed at least two days prior to implantation by ensheathing each with a six inch sleeve of polyester velour material cemented by silicone adhesive (GE RTV 112). Catheters were externalized along the spine between the scapulae, and buried in a closed subcutaneous pocket for

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later exteriorization. The burying procedure has resulted in the development of a good biological seal against bacterial invasion and prevented the development of descending sinus tract infections (unpublished data, White). Following two weeks of recovery, the pigs were refamiliarized with treadmill running for two weeks. At least two days prior to the first exercise tests, the catheters were exteriorized utilizing the same anesthetic techniques described above.

Cardiovascular and Temperature Measurements. A surface bipolar electrocardiogram (ECG) was recorded on a Hewlett-Packard 1511B ECG recorder. Heart rate (HR) was determined by manual measurement of the QRS to QRS interval. Arterial pressure was measured by a Statham P23ID transducer and recorded on a Brush 260 strip chart recorder. Rectal temperature was measured by a mercury thermometer before and after exercise.

Regional Blood Flow and Cardiac Output Measurements. Tissue blood flows were measured by the distribution of $4-5 \times 10^6$ 15 micron radiolabeled microspheres (New England Nuclear). Six labels (Cr_{51}, Sn_{113}, Ru_{103}, Nb_{95}, Sc_{46}, and In_{114}) were used for the blood flow determinations at rest and during EX using the technique of Heymann and Rudolph (14). Microspheres were suspended in a physiological saline solution containing 0.5% Tween 80. The microsphere suspension was injected into the left atrium after initiation of a reference sample withdrawal from the descending aorta. The cardiac output ($ml \cdot min^{-1}$) was calculated by the formula: [reference organ withdrawal rate ($ml \cdot min^{-1}$)] · [total isotope counts injected ($counts \cdot min^{-1}$)] · [reference organ counts ($counts \cdot min^{-1}$)]$^{-1}$ as described by Ishise (17). Stroke volume (SV) ($ml \cdot Kg^{-1}$) was estimated by dividing the cardiac output by the heart rate for each measurement.

Tissue Sampling. After the completion of all studies performed on each pig, euthanasia was performed with pentobarbital (100 $mg \cdot Kg^{-1}$). Portions of liver, spleen, stomach, small intestine, kidneys, brain, biceps femoris muscle, and left ventricular myocardium were harvested for analysis. Sampling of all tissues was not performed in all pigs. Six to eight gram (wet Wt.) tissue samples were weighed and dried. With this procedure, each counting vial contained a minimum of 400 spheres. Adequate mixing of each microsphere was assumed if less than a 15% difference existed between left and right renal or left and right brain BFs. The isotope spectra were separated on a Packard 591 spectrometer. An Apple IIe computer was used to perform inver-

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sion matrix calculations on the isotopic spectra and overlap ratios (39). This mathematical procedure provided the calculated blood flows for each tissue analyzed at the time of the measurements (injections).

The venous drainage of the splanchnic organs are collected by the hepatic portal vein. This portal vein BF (PV-BF) provides a major portion of the overall blood flow to the liver, with the remainder supplied by the hepatic artery (HA). Microspheres distributed initially to splanchnic organs are trapped in the capillary vasculature and do not reach the portal vein secondary collecting system (29). Thus, the microsphere technique determination of liver BF measures only the HA contribution to total liver BF. The stomach and small intestine BFs were assumed to be representative of the majority of the tissues which comprise the PV-BF and their average provided an estimate of PV-BF. The proportion of the total splanchnic blood flow passing through the liver was calculated by the ratio HA-BF:PV-BF. Since a measure of the total blood flow, and not just the flow per unit of tissue weight, are needed to evaluate overall splanchnic blood flow, this ratio provided only an indication of how the proportions of these blood flows were altered.

Exercise Protocol. Exercise tests were performed either after an 18-24 hour fast (FST) or 1-3 hrs post-feeding (FED), on a plexiglass sided motorized treadmill, and with room temperatures maintained at 21-23°C. The pigs were cooled by a fan. Variable time was allowed for individual pigs to achieve a resting state (HR<100 beats$\cdot$min^{-1} (BPM)) on the treadmill prior to the first measurement. Resting measurements were taken just prior to beginning the treadmill exercise protocol. Figure 1 illustrates the three minute stages of the progressive intensity exercise protocol (ramp test). Stages I and II were the same for all studies, with Stages III, IV, and V adjusted to attain the target heart rates of 225 BPM at Stage III for submaximal (S-MAX) and 275 BPM at Stage V for near-maximal (N-MAX) exercise. Relative work effort (% of Max) was calculated by the formula: ([Actual HR]-[Resting HR])$\cdot$([Maximal HR]-[Resting HR])$^{-1}$ (23). Based on a mean Maximal HR of 288 in untrained pigs (23), the target heart rates corresponded to approximately 70% and 95% of VO$_{2\ Max}$, respectively. However, the actual % of VO$_{2\ Max}$ for each exercise measurement may have varied due to individual variations in maximal HR and differences from the target HR. Heart rate, blood pressure, and regional BFs were measured in the last minute of each exercise stage. Regional blood flows were not measured at all exercise intensities on all

pigs. The stage speeds and grades were selected based on previous runs to provide equivalent HRs among pigs. Some pigs performed repeat tests 2-3 days after the first test.

Pre-Exercise Feeding. Nine pigs were fed their normal daily ration 1-3 hrs prior to the initiation of the studies to assess the effects of pre-exercise feeding (FED) on responses to exercise. The meal was approximately 3% of body weight of pig chow (1300 Kcal·lb^{-1}) consisting of 17% protein, 5% fat, and 78% carbohydrate. The work loads for these studies were adjusted to match heart rates attained during FST studies.

Statistical Analysis. Repeated measures analysis of variance was used to compare the three levels of exercise (REST, S-MAX, N-MAX), with FED vs. FST as the between group factor (6). Post hoc comparisons were performed using Newman-Keuls procedure (40). The level of significance was set at 0.05 for all comparisons. Values are presented as MEAN±Standard Error of the mean.

RESULTS

Summary of Two-Way MANOVA Results. The P values for the MANOVA tests are presented in Table 1. There was a significant effect of exercise intensity comparing REST, S-MAX, and N-MAX conditions for all variables, except liver (hepatic artery) blood flow (HA-BF) and the ratio of HA-BF to hepatic portal vein (PV) BF (HA-BF:PV-BF). There were significant effects of pre-exercise feeding on cardiac output, small intestine BF, and PV-BF, with a marginal effect on stomach BF. Based on these analyses post hoc comparisons were performed where applicable, with the results shown in Tables 2-4.

Cardiovascular Responses to Exercise. The heart rate (HR) rose progressively during the exercise (EX) protocol (Table 2, Figure 1) and corresponded to 67±0.4% and 94±0.4% of the heart rate reserve for S-MAX and N-MAX, respectively. The cardiac output (Figure 1) demonstrated a similar progressive rise while stroke volume, and mean arterial pressure increased from the resting value and plateaued between S-MAX and N-MAX. The mean exercise induced rise in rectal temperature was 1.1±.2°C, with a maximum range of 38.3 to 39.9°C for runs of 13.6±0.4 minutes duration (range: 9-15 min). The cardiac output was greater for FED than for FST at both S-MAX and N-MAX. The calculated stroke volumes for the FED condition were increased 10% and 16% over FST for S-MAX and N-MAX, respectively.

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Table 1. MANOVA results (P values) for two-way analysis of the effects of progressive intensity exercise (Intensity), effects of pre-exercise feeding (Food), and the interaction of those factors (Interact) on cardiovascular and tissue blood flow (BF) variables.

VARIABLE	Intensity	Food	Interact
Heart Rate	.00	.29	.32
Cardiac Output	.00	.02	.06
Stroke Volume	.00	.14	.08
Mean Arterial Pressure	.00	.22	.81
L. Ventricle BF	.00	.17	.11
Biceps Femoris BF	.00	.22	.50
Stomach BF	.00	.07	.12
Small Intestine BF	.00	.01	.04
Liver (HA) BF	.08	.19	.08
Spleen BF	.00	.56	.18
R. Kidney BF	.00	.72	.84
PV-BF(Estimate)	.00	.04	.18
HA-BF:PV-BF (Ratio)	.09	.32	.39

Intensity compared over three levels (Rest, Submaximal Exercise, and Near-Maximal Exercise). See other tables following for units of measure. Liver BF represents only the contribution of the hepatic artery (HA) to total liver BF, with the remainder supplied by the hepatic portal vein (PV).

Tissue Blood Flow Responses To Exercise. The left ventricular BF (Table 3, Figure 1) increased from rest to S-MAX, with no further increase at N-MAX. combining rest data with all exercise points, both HR and cardiac output (CO) ($ml \cdot min^{-1} \cdot Kg^{-1}$) were good predictors of myocardial (left ventricular) BF (LV-BF). the linear relationships were LV-BF ($ml \cdot min^{-1} \cdot 100g$ tissue^{-1}) = .91+.021·HR (N=71; r=.89; P<.001) and LV-BF = .19+.013·CO (N=68; r=.87; P<.001). the scatter plot of LV-BF vs. HR is shown in Figure 3. The biceps femoris BF increased progressively, while the stomach, small intestine (Figure 2), kidney, and portal vein BFs decreased progressively as exercise

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intensity increased. the biceps femoris BF was arithmetically lower for FED than for FST EX, but the difference was not significant (P=.22). The stomach and small intestine BFs were higher during FED than for FST EX. The liver showed no change in its arterial blood supply during fasting EX, but showed an increase at N-MAX during FED EX. These combined changes in liver BF during FST EX resulted in an overall decline in total liver BF (PV-BF+HA-BF) and an increase in the proportion of the total BF supplied to the liver by the HA (HA-BF:PV-BF) as EX intensity increased (Table 4). FED EX resulted in higher estimated PV-BFs, which provided a higher proportion of total liver BF than for FST EX.

Table 2. Effects of progressive intensity exercise on cardiovascular variables after an overnight fast (FST) and 1-3 hours after a meal (FED) based on post hoc analysis.

				EXERCISE	
VARIABLE		N	REST	S-MAX	N-MAX
Heart Rate	FST	25	93.8 (+3.3)+	221.7 (+3.3)	276.1 (+2.7)#
(Beats·min^{-1})	FED	8	101.8 (+8.5)+	230.0 (+5.8)	271.5 (+4.2)#
Cardiac Output	FST	21	88.8 (+1.9)+	262.1 (+8.6)	333.7(+11.8)#
(ml·min^{-1}·Kg^{-1})	FED	8	96.3 (+4.3)+	298.5(+11.9)&	381.7(+22.6)#&
Stroke Volume	FST	21	0.98(+.046)+	1.18(+.043)	1.21(+.046)
(ml·Kg^{-1})	FED	8	0.99(+.078)+	1.30(+.058)&	1.41(+.086)#&
Mean Arterial	FST	20	98.7 (+1.7)+	110.9 (+3.6)	117.1 (+3.5)
Pressure(Torr)	FED	8	95.5 (+1.9)+	105.2 (+1.6)	110.8 (+2.2)

Values MEAN (+SE). Significance: (P<.05). + = Rest different vs. both sub-maximal (S-MAX) and near-maximal (N-MAX) Exercise; $ = difference of either S-MAX or N-MAX vs. REST; # = N-MAX different vs. S-MAX; & = FED value is different from corresponding FST value.

Figure 1.   Three minute staged exercise test protocol, with Cardiac Output
and and Left Ventricle blood flow at Rest and during submaximal
(S-MAX) and near-maximal (N-MAX) exercise after fasting (FST) and
1-3 hours post-feeding (FED).   Values MEAN($\pm$SE), with significant
differences (p<.05) for: + = REST vs. EX (ALL); $ = vs. REST;
# = vs. S-MAX;   & = FST vs. FED (See Table 2 for further
explanation of statistical comparisons).

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Table 3. Effects of progressive intensity exercise on tissue blood flows after an overnight fast (FST) and 1-3 hours after a meal (FED) based on post hoc analysis.

TISSUE		N	REST	EXERCISE S-MAX	EXERCISE N-MAX
L. Ventricle	FST	13	116.5(+10.4)+	366.2(+22.1)	497.9(+36.8)
	FED	8	123.8(+14.5)+	453.6(+28.2)&	520.1(+40.9)
Biceps Femoris	FST	23	5.4 (+0.9)+	58.2 (+5.8)	84.7 (+8.6)#
	FED	8	4.5 (+2.4)+	47.0 (+5.8)	68.1 (+4.9)#
Stomach	FST	12	36.7 (+6.6)+	19.8 (+3.8)	7.8 (+1.8)
	FED	6	33.5 (+6.9)	29.6 (+7.5)&	13.7 (+1.2)$&
Small Intestine	FST	12	31.5 (+4.8)+	22.3 (+2.9)	10.6 (+2.1)#
	FED	7	65.0(+15.4)+&	38.0 (+7.4)&	17.8 (+2.0)#&
Liver (Hepatic Artery)	FST	11	10.2 (+2.5)	10.9 (+3.3)	12.3 (+3.6)
	FED	5	9.6 (+2.4)	11.1 (+3.4)	24.1 (+3.8)$&
Spleen	FST	12	236.7(+45.6)+	32.2 (+5.0)	20.0 (+7.3)
	FED	7	162.9(+28.5)+	46.4(+13.5)	36.9(+24.7)
R. Kidney	FST	16	404.7(+36.8)+	287.1(+35.2)	96.6(+26.6)#
	FED	5	382.8(+69.9)+	250.3(+33.9)	96.6(+26.9)#

Values MEAN (+SE) (ml·min^{-1}·100 gm^{-1}). Significance: (P<.05). + = vs. S-MAX and N-MAX; $ = vs. REST; # = vs. S-MAX; & = vs. FST. (See Table 2 for further explanation of statistical comparisons)

Table 4. Calculated effects of progressive intensity exercise on hepatic portal vein blood flow (PV-BF) and hepatic artery BF:PV-BF ratio (HA-BF:PV-BF) after an overnight fast (FST) and 1-3 hours after a meal (FED) based on post hoc analysis.

VARIABLE		N	REST	EXERCISE S-MAX	EXERCISE N-MAX
PV-BF	FST	12	32.6(+4.3)+	24.4(+4.5)	10.4(+1.6)#
(ml·min^{-1}·100g^{-1})	FED	6	51.6(+9.2)+&	35.6(+4.5)&	16.4(+1.0)#&
HA-BF:PV-BF	FST	8	0.42(+0.17)	0.80(+0.44)	3.16(+1.61)$'#'
	FED	6	0.22(+0.04)	0.23(+0.09)	1.36(+0.18)$'#'

Values MEAN (+SE) Significance: (P<.05). + = vs. S-MAX and N-MAX; $ = vs. REST; # = vs. S-MAX; & = vs. FST; EXCEPT: $' and #' indicate (P<.10). (See Table 1 for further explanation of statistical comparisons). PV-BF calculated from the average of stomach and small intestine BFs (Table 3); HA-BF:PV-BF (ratio) derived from the PV-BF/liver BF (Table 3).

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Figure 2. Stomach, Small Intestine, and Liver (hepatic artery) tissue blood flow responses to staged exercise after fasting (FST) and 1-3 hours post-feeding (FED). Values MEAN(+SE), with significant differences (p<.05) for: + = REST vs. EX (ALL); $ = vs. REST; # = vs. S-MAX; & = FST vs. FED (See Table 2 for further explanation of statistical comparisons).
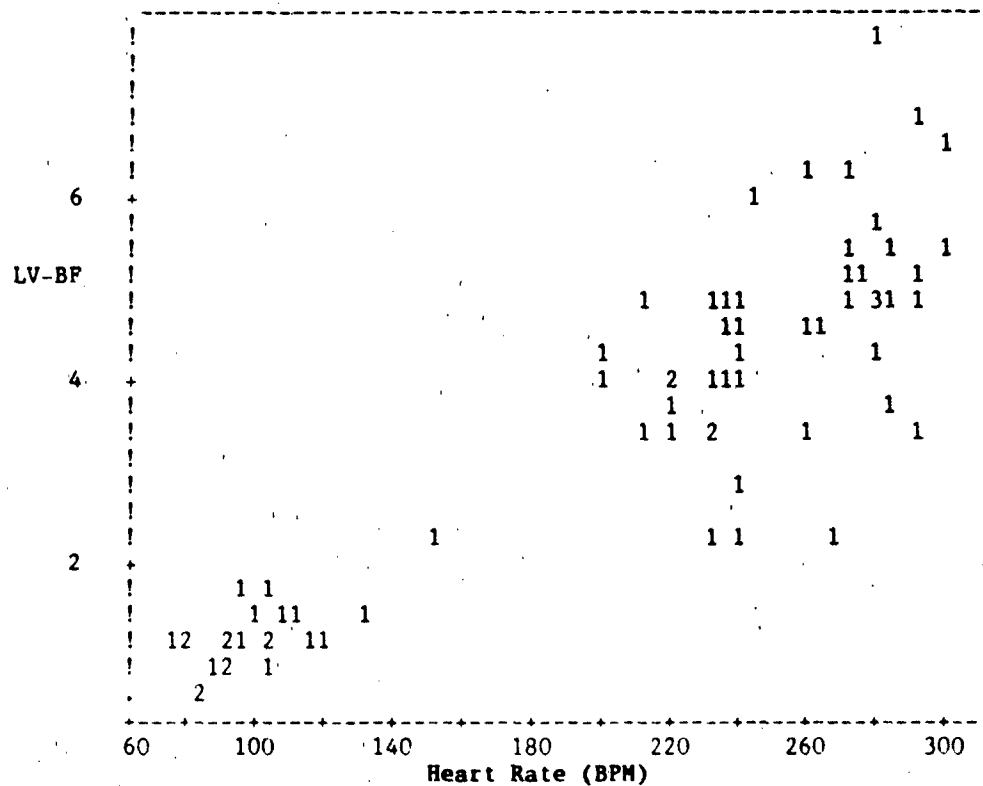
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       60    100    140    180    220    260    300
                        Heart Rate (BPM)
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Figure 3. Scatter plot and regression line of heart rate (BPM) versus left
ventricle blood flow (LV-BF)(ml·min^{-1}·100 gm^{-1}), including rest,
submaximal, and near-maximal exercise. The linear equation is
LV-BF = -.91127+.02141·HR (N=71; Regression Coefficient=.89;
P<.001).

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DISCUSSION

Exercise produces a substantial stress on the maintenance of cardio-vascular homeostasis, while other demands (e.g., hyperthermia, digestion) on the system may provide additional stress and increase the complexity of the homeostatic control problem. The effects of increasing exercise intensity on central cardiovascular and tissue blood flow (BF) responses will be addressed first. Second, the effects of feeding and the interactions of exercise and feeding will be discussed. Several apparent discrepancies in regional blood flow responses to exercise are examined by a systematic dissection of the factors which may have contributed to the differences in data. The effects of exercise duration on cardiovascular and BF readjustments will be discussed more completely in a subsequent paper (13).

Fasting Responses to Progressive Intensity Exercise. The mean of the stomach and small intestine BFs were used as an estimate of the relative change in portal vein BF (PV-BF) in the current data. The estimated PV-BF indicated there were progressive declines from rest of 32% at S-MAX and 73% at N-MAX. These decrements were accompanied by no change in hepatic arterial or liver BF (HA-BF). This alteration resulted in a progressive increase in the proportion of the total BF to the liver being supplied by the hepatic artery (HA-BF:PV-BF) (Table 4). However, the change in HA-BF:PV-BF was only an indicator of change, since this PV-BF estimate was based on the relative flow to the stomach and intestine and not on the total flow to the liver, as was the HA-BF. At a similar submaximal exercise intensity there were declines of 36% and 51% in the same tissues (proximal stomach and distal jejunum, respectively), or an average decline of 43.5%, at five minutes of exercise (13). Using the same calculations on these data (13), the HA-BF: PV-BF at rest and five minutes of exercise were 0.19 and 0.50, respectively. These values compare with 0.42 and 0.80, respectively, from the current data and indicates the calculated values of total gastrointestinal (GI) BF from our subsequent study compare well with those estimated from the current data. In this subsequent study the total splanchnic blood flow, summed by the weight of the individual organs at submaximal exercise, resulted in a 58% reduction in total calculated PV-BF and a 48% reduction in total liver (or splanchnic) BF after five minutes of exercise. These observed reductions in stomach and intestine BFs were similar to previous observations in pigs (23, 32) and man (30,31), but less than the reduction reported in pigs subjected

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to a more stressful exercise protocol (1). At N-MAX the estimated PV-BF had declined to 27% of the resting value, while the HA-BF was unchanged. This N-MAX estimate of GI BF in pigs compares very favorably to that reported in exercising man, where progressive reductions in total estimated splanchnic BF (ESBF) down to nearly 20% of normal were demonstrated at maximal effort (4,30,31). Conversely, untrained dogs showed widely variable declines among organ BFs during progressive intensity graded EX (24). Several studies in dogs reported little or no change in splanchnic BFs during EX (11,16,32,34).

Differences in EX intensity and duration (3,15,21,25,28,35) have added to the variability of results. Substantial variation in BFs to splanchnic tissues over time and responses among tissues (2,3,9,11,13,16,24) has further complicated comparisons among studies. Studies measuring BFs with comparable techniques and similar protocols indicate that both pigs and dogs exhibit declines in splanchnic BFs during exercise, but alterations measured in pigs from the current study and other reports (1,13,23,32) appear to more closely approximate those observed in man (30,31).

The mean arterial pressure (MAP) at REST for the current data (98.7 mmHg) was similar to some reports (13,32), but were substantially lower than the 115-123 mmHg reported for pigs in other studies (1,2,23,39). The increase in MAP between REST and N-MAX (19 mmHg) was comparable to that reported for pigs (1) and man (4,30), but less than other reported increments of 31-37 mmHg for pigs (23,32,39). Increases in MAP have been attributed to increases in regional vascular resistance for noncritical organs, such as splanchnic tissues (11) and may reflect a general level of stress. In our experience low anxiety and short periods of catheterization have substantially contributed to lower blood pressures at rest and in response to exercise.

The cardiac outputs from the current study compare favorably with those measured at similar work rates in untrained pigs (23,32,39) and in man (30), but were lower than those reported in trained pigs (13,23,39). Meaningful comparisons with other studies reporting cardiac outputs in dogs (3,9,11,16, 21,24,25,28), baboons (15), and man (4,5,18) have been difficult due to variations in units of measure and exercise conditions. Increments in stroke volume (SV) derived from exercise training (23,25,39) were responsible for the greater cardiac outputs at similar heart rates after training. We found an increase in SV between rest and exercise, with values very similar to those reported for man (30). In pigs we have demonstrated that contraction

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of the spleen or gastrointestinal capacitance vessels contributed to the increased blood volume (22) and potentially to stroke volume, while muscle pumping action has been the proposed mechanism in man (30). Other studies have described variable alterations in SV with EX, reporting no change (4,5,25,32), a decrease (4,11), or an increase (5, 9,15,18,24,32).

The increases in myocardial BFs as exercise intensity increased were similar to those reported in other comparable studies with pigs (1,13,23) and dogs (21,24,25,28), while somewhat less than other reports for pigs (32) and dogs (9,32). The current active muscle BFs were similar to values for dogs (9,28) at slightly lower heart rates and pigs (2,13,23) at similar heart rates. However, other studies have reported greater resting and maximal exercise muscle BFs ($ml \cdot min^{-1} \cdot 100g^{-1}$) in dogs (range: 142-316)(21,24,25,32) and pigs (1). Myocardial BFs may therefore be more similar among species than active muscle BFs due to variations in exercise protocols or to the muscles chosen for analysis (24). Based on the similarities in cardio-vascular and GI BF data between pigs and man discussed above, it is reasonable to infer that the myocardial and skeletal muscle BFs reported herein are also representative of those which would occur in man under similar exercise conditions. The correlations reported here data between either cardiac output (r=0.87) or HR (r=0.89) and left ventricular BF may therefore also be applicable to man. In general, our studies confirm previous reports that the central cardiovascular response to exercise of pigs compares more favorably to man than the dog (23,30,32).

Other factors may have contributed to differences in results among other studies. Exercise training status or exercise capacity of subjects may have influenced the variability of results. Previous data from well trained pigs suggested higher splanchnic BFs compared to untrained controls (23). Clausen et al. (5) reported a 7.2% higher ESBF after EX training in patients with coronary artery disease. Trained sled dogs (34) demonstrated almost no change in BF with sustained heart rates of 250-300 BPM for 2.5 hrs. However, no information on feeding status was provided in this report. Musch et al. (25) reported greater reductions in splanchnic BFs at maximal exercise in EX trained dogs than in untrained dogs (25), which contradicts other reports. BFs measured in endurance trained pigs at similar submaximal heart rates demonstrated lower myocardial and stomach BFs (13) than we observed in the current study, while small intestine and kidney BFs were higher, and liver

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and spleen BFs were similar. Differences between trained and untrained pigs suggests that training effects both the magnitude and pattern of changes in BF distribution in response to exercise. Species variation (25) and differences in training status among subjects may therefore have increased variability in the results of exercise studies.

Elevation in core temperature during steady state submaximal exercise has resulted in progressive increases in muscle BFs and variable changes in splanchnic tissue BFs (2). Similar progressive elevations in core temperature, which accompanied increments in work intensity, were reported by the same laboratory (1). However, a two hour submaximal exercise bout using trained pigs with a stable core temperature produced no progressive changes in either splanchnic or muscle BFs (13). In the current study the mean core temperature rise of $1.1^{\circ}C$ was less than the $1.5-2.3^{\circ}C$ elevations reported in two comparable studies (1,32). The greater elevations in temperature may have added to the observed increments in muscle and decrements in splanchnic BFs. The current results may have therefore been more reflective of a primary exercise effect on splanchnic BF without the overlay of thermal stress. Although thermal stress has produced added decrements in splanchnic BF (30, 31), many studies did not report thermal responses to EX (3,4,5,9,11,16,21, 23,24,25,34,35).

Differences among exercise protocols may have contributed to the variations in results (24). The current study utilized three minute staged increases in speed up to 3.1 MPH followed by increases in grade up to 17% (Figure 1). Similar blood flow responses were obtained by three minute increments in speed up to 4.3 MPH and grade increments to 15% (23,39). Using only two stages for submaximal (8 min) and severe exercise (32), or incrementing intensity with five minute intermittent stages (at 0% grade) by increasing speed up to 17.7 $Km \cdot hr^{-1}$ (1) produced different results, possibly due to differences in gait. Our (and others) experiences indicate that pigs are subject to hyperexcitability, particularly if they were not accustomed to handling. Additional variations in results between comparable protocols may have been caused by excitement induced sympathetic nervous system over-activity.

Four previous studies (1,23,32,39) utilized younger pigs (range: 4-7 months) than reported here (range: 9-12 months). Those studies (1,23,32,39) reported increments in heart rate similar to the current results as EX inten-

sity increased. Although age was a potential cause of the reported varia-
tions in BF results, the similarity of our data with results by McKirnan et
al. (23) using an identical protocol and younger pigs indicates differences
between the current data and other studies were probably not related to age.

Variations in measurement techniques and what they purportedly measure
might be responsible for misinterpretation of results. Previous studies
(1,2,9,15,21,23,24,25,26,28,32) as well as the current study employed micro-
sphere techniques to measure tissue BFs and, except for the inherent varia-
bility of the technique, these studies should be comparable. Other studies
utilized flow probes to measure arterial BFs (3,11,16,34,35,36,37) or indica-
tor elimination techniques to estimate total liver (splanchnic) blood flow
(4,5,30,31). The problems of comparison between flow probe, microsphere, and
indicator elimination techniques have been previously discussed (11,25,30).
Results from these various techniques are sometimes difficult to compare.
However, the similarity of the current data with the indicator elimination
techniques used in human subjects (30,31) provides an encouraging comparison.

Lastly, reports for pigs (1,2,32) and other subjects (4,9,24,28,34) have
provided no information on feeding status at the time of exercise. The
variation in results potentially imposed by pre-exercise feeding are
addressed below.

Effect of Feeding on Responses to Progressive Intensity Exercise. Feed-
ing resulted in increased small intestine (Table 3) and PV-BF (Table 4) at
rest. These data are in agreement with previous reports of postprandial
mesenteric hyperemia (3,7,11,13,16,26,27,33,36,37). These data from
untrained pigs compared well with postprandial elevations of 4-10 BPM in dogs
(11,36) and man (12,18), while there was no difference due to feeding in
endurance trained pigs (13). These data support a slight increase in total
cardiovascular demand to meet the added metabolic requirements of digestion.

The tissue blood flow and cardiovascular responses to progressive post-
prandial (FED) exercise were somewhat different than those measured under
fasting (FST) conditions. Feeding produced significant effects on left
ventricular, stomach, small intestine, and liver BFs. The stomach and small
intestine BFs declined progressively from resting values as exercise inten-
sity increased from S-MAX to N-MAX, but remained elevated compared to the
corresponding FST values. Interestingly, the FED liver BF showed no change
from REST to S-MAX, but exhibited a dramatic increase at N-MAX. The eleva-

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tion in FED liver BF at N-MAX corresponded to stomach and small intestine BFs, which, although reduced from S-MAX levels, were higher than the FST values. These data agree with those obtained during submaximal exercise in our subsequent study utilizing trained pigs (13). The estimate of portal vein BF (PV-BF) in the current report demonstrated an elevation in PV-BF at all time points during FED exercise. A study with dogs similarly demonstrated that the increase in total liver BF resultant from eating was primarily from an increase in PV-BF (16) and this difference was maintained during exercise. The elevated FED exercise BFs resulted from a combination of local blood flow control mechanisms (7,29,38,41) which acted to maintain sufficient BF to meet local metabolic requirements. Other studies have shown that FED exercise produced no effects on gastric acid secretion (8), gastric emptying, or food absorption (8,10) for moderate EX of 45-60 minutes in duration. Additional variations in BF responses have also resulted from differences in meal composition (27,33,37). The meal fed to the pigs in the current study was mostly carbohydrate (78%). A meal higher in protein or fat, such as meat meals fed to dogs, might reasonably be expected to have produced greater differences from the fasting condition.

The increase in FED liver BF at N-MAX may have been a physiological demonstration of the previously described 'hepatic arterial buffer response' (20). This buffer response is a proposed mechanism by which the liver maintains its total blood flow with compensatory increases in hepatic artery BF if portal vein BF declines. Liver BF patterns suggestive of the buffer response have resulted from feeding (26), submaximal exercising pigs (13), and maximal exercising dogs (21) and pigs (1,23,32). Previous studies with dogs (3,11,16) also demonstrated higher splanchnic BFs during FED exercise, while others reported no change from resting BFs (16,36). No directly comparable studies have been reported for pigs.

Variation in BF response to a meal over time (3,7,11,16,26,37), coupled with variations in BF response from EX result in a very complex overlay of systemic stresses, where the timing of measurements may also result in wide variations of responses. The differences between FST and FED responses to EX in splanchnic tissue BFs were observed in both magnitude and in pattern of alteration. As previously discussed, due to the similarities in fasting responses of pigs and man to fasting exercise, it is reasonable to speculate that man would have a similar postprandial exercise splanchnic BF responses.

Skeletal and cardiac muscle demonstrated variable effects due to feeding. The FED myocardial BFs were arithmetically greater for all exercise conditions, but the difference was only significant at S-MAX. These differences were difficult to interpret, since the work loads were adjusted to match heart rates. The higher FED S-MAX myocardial BF was associated with arithmetically higher, but not significantly elevated heart rate. In our subsequent study (13), utilizing matched absolute work loads for FST and FED runs, the myocardial BFs were lower in the FED condition. There have been no other comparable microsphere studies on the effects of feeding on myocardial BF. The active muscle BF (biceps femoris) was numerically, but not significantly (P=.22) lower for the FED condition. As previously noted above, a study in dogs using flow probes demonstrated a relative increase in iliac artery vascular resistance during FED exercise compared to FST (11). Lower hindlimb muscle blood flows for FED than for FST moderate intensity EX have also been demonstrated (13). A decrease in muscle perfusion without any compromise in arterial blood pressure is indicative of increased sympathetic tone in the muscle vascular bed (30). It is fair to summarize from these studies that by either matching absolute work load or matching heart rates, the myocardial blood flow responses observed during postprandial exercise are different than those observed during exercise under fasted conditions.

Central cardiovascular responses to exercise were also effected by feeding. S-MAX FED exercise produced no differences in HR compared to FST in dogs (11), 10 BPM higher heart rates in man (12,18), but lower HRs in endurance trained pigs (13). These previous studies were conducted at matched work loads (11,12,13,18,36) and are not directly comparable. However, it would be reasonable to expect that postprandial heart rates would be higher due to the increased cardiovascular demands of the digestive process. The opposite effect of lower HRs during FED S-MAX postprandial exercise may be a result of exercise training (13).

There was no change in MAP at rest for fed dogs (36), while others reported transient increases of 10-20 torr in dogs (11) and baboons (37) that returned to normal after 30 minutes (37). FED exercise in dogs produced transient increases in MAP during the first minute with a return to normal (36) or an increase (10 torr) which persisted for the four minutes of exercise (11). Increases in MAP have been related to increased sympathetic tone associated with the activity of eating (11), while reductions have been

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attributed to reduced splanchnic tissue vascular resistance observed after eating (9,11,36,37) and during FED exercise (11) compared to FST. The combined and opposing effects of eating and exercise on MAP are difficult to predict due to competing adjustments in resistance to the various vascular beds.

The FED cardiac output (CO) was unchanged from FST at rest, but greater at both S-MAX and N-MAX in the face of similar heart rates. These data are comparable to unchanged FED COs at rest in dogs (3,11,36), while men had a 16% increase (18) and pigs were unchanged (13) at rest. Dogs exhibited a similar increase in magnitude of CO from the resting value for FED exercise as compared to FST (3,11), but the FED COs were surprisingly lower than for the FST runs. However, the control of exercise intensity was not specified in these studies (3,11) and may have effected the results. S-MAX exercise in pigs (13) resulted in a greater CO for FED than for FST at all but one time point during prolonged exercise. A study with human subjects reported higher COs during postprandial exercise than during FST exercise (18), but the intensity and controls were not well defined.

From the combined information, it is reasonable to conclude that post-prandial S-MAX exercise produces a greater cardiac output than equivalent work load fasting EX. There is an apparent interaction between exercise and feeding which alters the normal fasting cardiovascular and regional blood flow responses to exercise. However, true maximal CO is not likely to be affected by the feeding status of the individual. These data suggest the increased sympathetic tone which accompanies exercise (11) is overridden by local gastrointestinal mechanisms (6,29,38,41) active during FED exercise. These local regulatory mechanisms provide ascending feedback signals to the central nervous system by way of the predominantly afferent vagus nerve (41). It would appear that when the additional stress of exercise is superimposed upon the digestive demands, both the magnitude and pattern of response of the entire cardiovascular and blood flow distribution system is altered. These coincident changes provide an additional impetus to the concept that a central neurogenic mechanism is responsible for the change in cardiovascular dynamics as suggested in the previous section.

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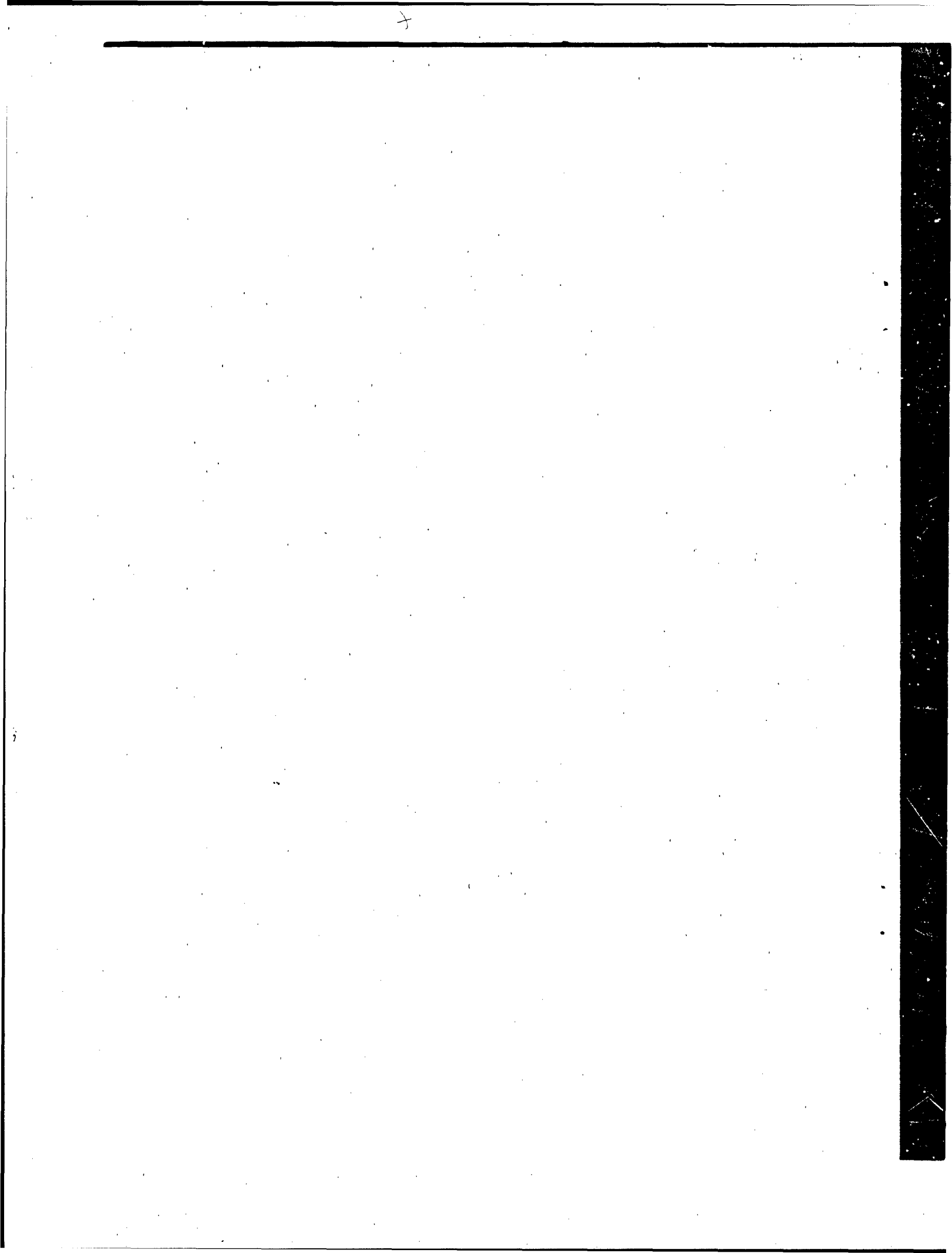
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REPORT DOCUMENTATION PAGE

1a REPORT SECURITY CLASSIFICATION	1b RESTRICTIVE MARKINGS
Unclassified	N/A

2a SECURITY CLASSIFICATION AUTHORITY	3 DISTRIBUTION / AVAILABILITY OF REPORT
N/A	Approved for public release; distribution unlimited
2b DECLASSIFICATION / DOWNGRADING SCHEDULE	
N/A	

4 PERFORMING ORGANIZATION REPORT NUMBER(S)	5 MONITORING ORGANIZATION REPORT NUMBER(S)
NHRC Report N. 88- 31	

6a NAME OF PERFORMING ORGANIZATION	6b OFFICE SYMBOL (If applicable)	7a NAME OF MONITORING ORGANIZATION
Naval Health Research Center	70	Commander, Naval Medical Command

6c ADDRESS (City, State, and ZIP Code)	7b ADDRESS (City, State, and ZIP Code)
P.O. Box 85122 San Diego, CA 92138-9174	Department of the Navy Washington, DC 20372

8a NAME OF FUNDING / SPONSORING ORGANIZATION Naval Medical Research & Development Command	8b OFFICE SYMBOL (If applicable)	9 PROCUREMENT INSTRUMENT IDENTIFICATION NUMBER

8c ADDRESS (City, State, and ZIP Code)	10 SOURCE OF FUNDING NUMBERS			
Naval Medical Command National Capital Region Bethesda, MD 20814-5044	PROGRAM ELEMENT NO	PROJECT NO	TASK NO	WORK UNIT ACCESSION NO

11 TITLE (Include Security Classification)
EFFECTS OF EXERCISE INTENSITY AND PRE-EXERCISE FEEDING ON SPLANCHNIC TISSUE BLOOD FLOW

12 PERSONAL AUTHOR(S)
Gray, Chas. G.; White, Francis, C.; McKirnan, M. D.; Lawlor, M. R.; Bloor, C. M.

13a TYPE OF REPORT	13b TIME COVERED	14 DATE OF REPORT (Year, Month, Day)	15 PAGE COUNT
Interim	FROM ___ TO ___	1988AUG23	

16 SUPPLEMENTARY NOTATION
Prepared in cooperation with the Department of Pathology, University of California, San Diego, School of Medicine.

17	COSATI CODES		18 SUBJECT TERMS (Continue on reverse if necessary and identify by block number)
FIELD	GROUP	SUB-GROUP	Progressive exercise; Hemodynamics; Splanchnic blood flow; Muscle blood flow; Microspheres; Feeding; Postprandial

19 ABSTRACT (Continue on reverse if necessary and identify by block number)
Tissue blood flows (BFs) and cardiovascular variables were studied in thirty 9-12 month old Yucatan miniature swine subjected to a progressive exercise treadmill run after an overnight fast (FST) or one to three hours post-feeding (FED). Radiolabeled microspheres were used to measure tissue BFs and cardiac outputs (COs) at rest and during submaximal (S-MAX) and near-maximal (N-MAX) exercise in untrained pigs. Relative workloads were 67 (+0.4)% and 94 (+0.4)% (Mean+SE) of the heart rate reserve for S-MAX and N-MAX, respectively. Progressive exercise for both FST and FED animals resulted in incremental elevations in CO and mean arterial pressure (MAP), with coincident increments in myocardial and muscle BFs. Fasting BFs (ml·min^{-1}·100g^{-1}) at rest for the stomach (36.7+6.6), small intestine (31.5+4.8), spleen (236.7+45.6), and kidney (404.7+36.8) declined progressively to 7.8+1.8, 10.6+2.1, 20.0+7.3, and 96.6+26.6, respectively at N-MAX. Liver BF was 10.2+2.5 at rest and was not altered by exercise. FED exercise produced responses somewhat different from FST. The FED COs (ml·min^{-1}·Kg^{-1}) of 298.5+11.9 at S-MAX and 381.7+22.6 at N-MAX were greater (p<.05) than the corresponding FST values by 7.2% and 5.5%, respectively. The greater CO for FED N-MAX (over)

20 DISTRIBUTION / AVAILABILITY OF ABSTRACT	21 ABSTRACT SECURITY CLASSIFICATION (over)
☐ UNCLASSIFIED/UNLIMITED ☒ SAME AS RPT ☐ DTIC USERS	Unclassified
22a NAME OF RESPONSIBLE INDIVIDUAL Charles G. GRAY	22b TELEPHONE (Include Area Code) (619) 553-8453	22c OFFICE SYMBOL 70

DD FORM 1473, 84 MAR
83 APR edition may be used until exhausted
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SECURITY CLASSIFICATION OF THIS PAGE

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19. ABSTRACT (continued)

was associated with a greater stroke volume than for FST (p<.05). The FED left ventricular BF at N-MAX (520 ± 40.9 ml$\cdot$min$^{-1}\cdot$100g^{-1}) was the same as for FST. There was a high correlation (.87) between CO and HR and left ventricular BF. The stomach and small intestine BFs were greater for FED exercise than for FST exercise. FED liver BF exhibited an increase (p<.05) from 9.6 ± 2.4 at rest to 24.1 ± 3.8 at N-MAX. FED differed from FST exercise in both the magnitude and pattern of change from rest in cardiovascular variables and tissue blood flows. The integration of these and previous data observed during FED exercise suggest that a neurogenic autonomic reflex of gastrointestinal origin may be active in minimizing blood flow to active muscle organs when the coincident stress of digestion is superimposed on the stress of exercise. These data indicate the potential importance of controlling for food intake when any cardiovascular functions are of interest.